

## ABSTRACT

The present invention provides methods, compositions and kits for highly efficient, high throughput detection of mutation or nucleotide variation of an organism. By exploiting the molecular interactions between strands of nucleic acid and between nucleic acid and protein, assays have been developed to detect nucleotide variation, in particular, single nucleotide polymorphism (SNP) in various biological samples including human genomic DNA and virus. In preferred embodiments, immunoassays are developed to specifically capture a nucleic acid-protein complex formed between a 4-way nucleic acid structure called Holliday junction and a protein that specifically recognizes the Holliday junction. These assays can be used in a wide variety of applications such as diagnostics, genotyping, genetic profiling, mutation detection, disease prevention, therapeutic treatment, and screening for therapeutic targets or therapeutics.